Recommendations by the Quality Task Group (102)

Low-temperature sterilization processes

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1 Introduction

For medical device (MD) reprocessing there are various processes that must be taken into account. The continuous, rapid pace of developments in medical technology is driving the introduction of ever more complex systems and medical devices, which in turn make increasingly more stringent demands on reprocessing. For example, there is a sharp rise in the number of ➜ **THERMOLABILE** (heat-sensitive) MDs, such as flexible endoscopes, camera heads, ultrasonic transducers and electronic sensors, which can only be sterilized with low-temperature processes.

➜ **THERMOLABILE MD** can only be sterilized with low-temperature processes.

Even the preceding cleaning and disinfection steps are carried out at lower temperatures for the material compatibility reasons mentioned. Instead of the normally used thermal disinfection (e.g. A_0 3000 – at around 90 °C), chemothermal disinfection (addition of a disinfectant) is employed at temperatures of generally less than 60 °C.

Likewise, instead of the generally more popular steam sterilization process at temperatures of 134 °C, for sterilization of heat-sensitive medical devices low-temperature sterilization at much lower temperatures (e.g. 50 – 70 °C) is used.

In the medical setting in Germany, Austria and Switzerland the following ➜ **LOW-TEMPERATURE PROCESSES** are employed:

➜ **LOW-TEMPERATURE PROCESSES** used in the medical setting.

- Hydrogen peroxide sterilization with and without a plasma phase
- Low-temperature steam and formaldehyde sterilization (LTSF)
- Ethylene oxide sterilization
- Gamma irradiation (industrial production)

If necessary, prionicidal activity must be taken into consideration. The KRINKO/BfArM Recommendation* 2012, Annex 7, sets out measures to curtail the risk of transmission of CJD/vCJD via medical devices.

Other factors, e.g. cycle times, chamber volume, sterilization temperature, running costs (such as maintenance and validation) and energy costs, should be taken into account at the time of procurement.

2 Processes

2.1 Hydrogen peroxide sterilization with and without a plasma phase

Hydrogen peroxide sterilization

Hydrogen peroxide sterilization is a low-temperature sterilization process with activity in temperature ranges below 60 °C. Most sterilizers operate at a temperature of around 50 °C – 55 °C.

The cycle times chosen will depend on the respective system (sterilizer model and design) as well as on the design of the MD (lumen, length, materials). The information supplied by the sterilizer manufacturer and the reprocessing instructions for the specific medical device must be observed. Instrument compatibility with the sterilization process and intended programme must be evaluated and a written record of that kept. Partial prionicidal activity has been demonstrated for a number of processes (see also the aforementioned KRINKO/BfArM Recommendation, Annex 7).

* KRINKO/BfArM Recommendation*: Recommendation for hygienic processing practices for medical devices, jointly compiled by the Commission for Hospital Hygiene and Infection Prevention at the Robert Koch Institute (RKI) and the Federal Institute for Drugs and Medical Devices (BfArM)

➜ **ADVANTAGES** of hydrogen peroxide sterilization

Hydrogen peroxide sterilization has the following ➜ **ADVANTAGES**:
- Good material compatibility
- Sterilant activity within a sterile container and/or soft packaging
- Easy and safe handling
- Short batch times
- No water consumption

Hydrogen peroxide sterilization is a low-temperature process operated at negative pressure. Hydrogen peroxide (H_2O_2), the sterilant, is present in the process in gaseous form. This gaseous environment enhances the oxidizing properties of H_2O_2 promoting the formation of free radicals endowed with potent biocidal activity. If a plasma phase is incorporated, it generally provides for conditioning of the sterile supplies and/or inactivation of the remaining H_2O_2 or its remaining free radicals.
Few technical requirements apply here. This is a closed system that generally requires only a power connection. During the process it must be ensured that the sterilant is able to access all internal and external surfaces. In terms of health and safety, no additional permit is needed for operation of a H_2O_2 process.

2.2 Low-temperature steam and formaldehyde (LTSF) sterilization processes

LTSF sterilization is a low-temperature sterilization process based on the use of a formaldehyde-steam mixture in temperature ranges of around 60 – 70 °C .The sterilant activity derives from a reaction with protein groups in the cells of microorganisms. In Germany, the Hazardous Substances Regulation (GefStoffV Section 7(3) of 26 November 2010) and the German Technical Regulations on Hazardous Substances (TRGS) 513 must be observed.
The cycle times chosen will depend on the respective system (sterilizer model and design) as well as on the design of the MD (lumen, length, materials). The information supplied by the sterilizer manufacturer and the reprocessing instructions for the specific medical device must be observed.

➜ **ADVANTAGES** of LTSF sterilization

LTSF sterilization has the following ➜ **ADVANTAGES**:
- Good material compatibility
- Sterilant activity within a sterile container and/or soft packaging
- Easy and safe handling
- Acceptable batch times
- Cost-effective process (procurement and operation)

In the sterilizer the formaldehyde solution is conveyed immediately to the steam generator, i.e. directly into the sterilization chamber without any contact with the outer regions of the sterilizer. Unlike a steam sterilizer, in the LTSF sterilizer there are essentially more load changes (fractionated prevacuum/pulsed vacuum method).
On completion of the process steps: formaldehyde injection (several fractionation cycles and holding time), desorption (several fractionations in which the steam is separated from the formaldehyde) and drying, the medical device can be safely withdrawn from the sterilizer. During the process it must be ensured that the sterilant is able to access all internal and external surfaces.
Based on the currently valid Hazardous Substances Regulation no permit is needed for a fully automated sterilizer for medical use, with a chamber volume of less than 1 m^3 and which complies with the state of the art (e.g. DIN EN 14180).
The structural requirements are similar to those applicable to steam sterilization.

2.3 Ethylene oxide sterilization

➜ **ETHYLENE OXIDE STERILIZATION** is mostly used in industrial settings.

➜ **ETHYLENE OXIDE STERILIZATION** is used for low-temperature sterilization in industrial settings and increasingly less in the healthcare sector. The sterilant action of ethylene oxide in combination with water derives from a change in the protein molecules in the cells of microorganisms. Both positive- and negative-pressure processes are employed. Modern sterilizers use a mixture of 6% ethylene oxide and 94% carbon dioxide since at normal pressure this mixture is no longer flammable. In Germany, the Hazardous Substances Regulation (GefStoffV Section 7(3) of 26 November 2010) as well

as the Technical Regulations on Hazardous Substances (TRGS) 513 must be observed. Following ethylene oxide sterilization, desorption, or degassing, must be carried out to release the ethylene oxide that had penetrated, or adsorbed on, the devices during sterilization. The desorption time will depend on the composition of the MDs being sterilized and on the packaging (the manufacturer's instructions must be noted).
In addition to the technical requirements to be borne in mind for steam sterilization, a catalytic converter is needed for the exhaust air as well as at least six air exchanges in the installation room for compliance with the provisions of the German Technical Instructions on Air Quality Control (TA Luft).

3 Validation and routine monitoring

3.1 Hydrogen-peroxide sterilization with and without a plasma phase

Here the provisions specified in the "superordinate/higher-level" standard DIN EN ISO 14937 must be observed since, to date, there is no dedicated ➜ **STANDARD** for validation and routine monitoring of this sterilization process. The Cleaning, Disinfection and Sterilization Horizontal Working Group of the German Central State Body for Health Protection with Regard to Drugs and Medical Devices (ZLG) has published a document setting out minimum requirements. This is entitled "RDS 004 – Minimum Content of Validation Reports for Peroxide/Peroxide Plasma Sterilization Processes for Medical Devices".

➜ **THERE IS NO DEDICATED STANDARD** for H_2O_2 sterilization processes. The provisions specified in the superordinate standard EN ISO 14937 must therefore be observed.

3.2 Low-temperature steam formaldehyde sterilization (LTSF)

Validation and routine monitoring of LTSF sterilization processes is conducted pursuant to DIN EN 14180 and DIN EN ISO 25424. Test loads are used to demonstrate the efficacy of the process.
In 2009, the German Society of Hospital Hygiene (DGKH) published a ➜ "**RECOMMENDATION** for validation and routine monitoring of sterilization processes with formaldehyde-containing steam for medical devices".

➜ **A RECOMMENDATION** for validation and routine monitoring of LTSF sterilization processes has been published by the German Society of Hospital Hygiene (DGKH).

3.3 Ethylene oxide sterilization

Validation of ethylene oxide sterilization processes in industry is an integral component of the quality management system. The standard regulating validation and routine monitoring is DIN EN ISO 11135. DIN EN ISO 10993-7 regulates the residual gas concentration.
No further details are given here on validation of this process since it is now rarely used in healthcare institutions.

4 Packaging

A distinction is made between soft and hard packaging. ➜ **SOFT PACKAGING** may be made of paper, paper/foil, smooth and crepe paper, nonwovens, SMS and Tyvek®.
➜ **HARD PACKAGING** refers to a container (sterilization container) made of chrome steel, aluminium or solid plastic. The packaging requirements are regulated by DIN EN ISO 11607

➜ **SOFT PACKAGING** may be made from different materials.
➜ **HARD PACKAGING** refers to sterilization containers.

4.1 Packaging for hydrogen peroxide sterilization with and without a plasma phase

Packaging for hydrogen peroxide sterilization

4.1.1 Soft packaging

Transparent packaging made of polyethylene/polyester composite film and Tyvek whose suitability has been confirmed by the manufacturer of the sterilizer and packaging materials. This may be available as a single or double wrapper

4.1.2 Hard packaging

These are containers whose suitability has been confirmed by the manufacturer of the sterilizer and packaging materials.

4.2 Packaging for LTSF sterilization

Packaging for LTSF sterilization

4.2.1 Soft packaging

– Paper and crepe paper
– Nonwovens with cellulose component

– SMS made of 100% polypropylene
– Transparent packaging made of paper or nonwoven material with PET/PP foil
– Transparent packaging made of Tyvek and PET/PE

Only soft packaging whose suitability has been confirmed by the manufacturer of the sterilizer and packaging materials is used.

4.2.2 Hard packaging

These are containers whose suitability has been confirmed by the manufacturer of the sterilizer and packaging materials.

4.3 Packaging for EO sterilization

4.3.1 Soft packaging

– Paper and crepe paper
– Nonwovens with cellulose component
– SMS made from 100% polypropylene
– Transparent packaging made from paper or nonwovens with PET/PP foil
– Transparent packaging made from Tyvek and PET/PE

Only soft packaging whose suitability has been confirmed by the manufacturer of the sterilizer and packaging materials is used.

4.3.2 Hard packaging

Only containers whose suitability has been confirmed by the manufacturer of the sterilizer and packaging materials are used.

Table: Compatibility with the sterilization process

	STEAM (steam)	EO (Ethylene oxide)	FORM (Formaldehyde)	VH_2O_2 (vaporized hydrogen peroxide)	Dry heat (hot air)
Paper (paper bags, crepe paper)	YES	YES	YES	No	No
Nonwovens with cellulose component	YES	YES	YES	No	No
SMS Material made of 100% PP	YES	YES	YES	YES	No
Transparent packaging made of paper or nonwoven material with PET/PP foil	YES	YES	YES	No	No
Transparent packaging made of Tyvek® and PET/PE	No	YES	YES	YES	No
Container*	YES	YES	YES	YES	No

(Source: Recommendation by the Quality Task Group No. 79 – Central Service 3/2013)
*Evidence of the intended sterilization process must be available

5 References

1 Verordnung zum Schutz vor Gefahrstoffen (Gefahrstoffverordnung – GefStoffV).
2 Technische Regeln für Gefahrstoffe – TRGS 513 «Tätigkeiten an Sterilisatoren mit Ethylenoxid und Formaldehyd.»
3 KRINKO/BfArM-Empfehlung «Anforderungen an die Hygiene bei der Aufbereitung von Medizinprodukten»
4 DIN EN ISO 10993-7 «Biologische Beurteilung von Medizinprodukten – Teil 7: Ethylenoxid-Sterilisationsrückstände»
5 DIN EN ISO 11135 «Sterilisation von Produkten für die Gesundheitsfürsorge - Ethylenoxid – Anforderungen an die Entwicklung, Validierung und Lenkung der Anwendung eines Sterilisationsverfahrens für Medizinprodukte»
6 DIN EN ISO 11607-1 «Verpackungen für in der Endverpackung zu sterilisierende Medizinprodukte – Teil 1: Anforderungen an Materialien, Sterilbarrieresysteme und Verpackungssysteme»
7 DIN EN ISO 11607-2 «Verpackungen für in der Endverpackung zu sterilisierende Medizinprodukte – Teil 2: Validierungsanforderungen an Prozesse der Formgebung, Siegelung und des Zusammenstellens»
8 DIN EN ISO 14180 «Sterilisatoren für medizinische Zwecke – Niedertemperatur-Dampf-Formaldehyd-Sterilisatoren – Anforderungen und Prüfung»
9 DIN EN ISO 14937 «Sterilisation von Produkten für die Gesundheitsfürsorge – Allgemeine Anforderungen an die Charakterisierung eines sterilisierenden Agens und an die Entwicklung, Validierung und Lenkung der Anwendung eines Sterilisationsverfahrens für Medizinprodukte»
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11 HAK RDS 004 «Mindestinhalte von Validierungsberichten für Peroxid/Peroxid-Plasma-Sterilisationsverfahren für Medizinprodukte»,Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten (ZLG), Horizontales Arbeitskomitee Reinigung, Desinfektion und Sterilisation (HAK RDS)
12 Handbuch Sterilisation – von der Reinigung bis zur Bereitstellung von Medizinprodukt Guido Wismer – Aarau/Toni Zanette, mhp Verlag,Wiesbaden, ISBN 978-3-88681-129-8
13 Deutsche Gesellschaft für Krankenhaushygiene e.V. (DGKH) «Empfehlung für die Validierung und Routineüberwachung von Sterilisationsprozessen mit formaldehydhaltigem Wasserdampf nach dem NTDF-Verfahren (Niedertemperatur Dampf und Formaldehyd) für Medizinprodukte»
14 Wallhäußers Praxis der Sterilisation, Antiseptik und Konservierung: Qualitätssicherung der Hygiene in Industrie, Pharmazie und Medizin; Hrsg. Axel Kramer, Ojan Assadian, Thieme Verlag, Stuttgart, ISBN 9783131411211